REMARKS

Claims 1-24 are all the claims pending in the application.

Claim 24 is canceled without prejudice in view of the restriction requirement and the Applicants retain the right to pursue Claim 24 in a Divisional application. Claims 19-23 have been amended to correct typographical errors. The amendments to Claims 1 and 2 add the word "modified" and Claims 14 and 15 have been amended to add a regeneration step. None of the amendments represent the addition of new matter. Support for the amendment to Claims 1 and 2 can be found throughout the Specification and in particular in (a) Section 5.2 where the location and types of mutations (changes) in the EPSPS genes are described and the original claims that specify a mutant EPSPS gene. Support for the regeneration step in Claims 14 and 15 can be found on page 1, line 20, Section 3 Summary of the Invention and Section 5 Detailed Description of the Invention.

Information disclosure Statement

Reference B1, a German language patent document, has a US equivalent US Patent 5,750,673. The only relevance of this reference is that it discloses modified RNA molecules and the fact that the present recombinagenic oligonucleotides may contain modified RNA.

Drawings

A copy of the corrected drawings sent under separate cover to the Draftsperson is enclosed for the Examiner's review.

101 Rejection

Claims 1-13 have been rejected under 35 USC 101 for covering non-statutory subject matter. This rejection is deemed moot in view of the

transgenic plant" to exclude the claims from covering natural mutations. Withdrawal of this rejection is respectfully requested.

112 Rejection – Indefiniteness

Claims 14-22 have been rejected under 112, 2nd paragraph, for not containing a regeneration step and having incorrect dependency language in Claims 20-22. This rejection is also deemed moot in view of the amendments made to these claims. Claims 14 and 15 have been amended to include a regeneration step "c" and Claims 20-23 have been amended to depend upon the "method Claims" instead of the incorrect "plant claims." Withdrawal of this rejection is also respectfully requested.

112 Rejection – Enablement

Claims 1-23 have been rejected under 35 USC 112, first paragraph, for not being enabling. The Examiner states that the Applicants have taught that the Specification teaches producing EPSPS mutants and transforming them into bacteria instead of the claimed method of producing plants. This rejection is respectfully traversed.

The Applicants merely use an "*in vitro*" bacterial expression system to demonstrate that (1) the gene products of the *Arabidopsis* mutant genes are in fact glyphosate resistant and allowed the host to grow in a manner substantially the same as wild-type cells (See Fig 6) and (2) the mutant *Arabidopsis* clones expressed the mutant protein at substantially the same level as the wild-type protein (See Fig 7). The Applicants have provided detailed sequence information that identifies the EPSPS gene and mutants for *Arabidopsis thaliana, Brassica napus, Petunia hybrida and Zea mays* (See Section 4 of the Specification). The Applicants have further given great detail on the use of the recombinagenic oligonucleobase (gene repair) technology that is used in combination with the sequence information to make the specific desired mutations in plant cells.

[illegible] that this technology works time in this art. In

fact, taken in context of the know-how of one of ordinary skill in **this** art these two articles do in fact demonstrate that the Applicants have enabled the present claims. The Applicants should not be penalized for a relatively high degree of skill compared to other arts that have a relatively lower level of skill. One of ordinary skill in the art is only deemed to have to do his job the old fashioned way –namely, do the experiments (akin to making money the old fashioned way by **earning** it). The fact that doing plant genetic engineering takes time (at least months and sometimes years for certain plant species) as opposed to, say, a chemical reaction in a beaker that may take minutes, hours or even overnight is not a reason to penalize or discriminate against plant biologists in the Patent Office. The Applicants have identified several EPSPS sequences, shown several areas in the sequence that should be mutated, and taught how to change the target nucleotides with recombinagenic oligonucleobases and recover modified, non-transgenic plants. It is well within the purview of the skilled artisan to do a routine test to confirm that the mutation has occurred in the proper place. As of the filing date of this application sequence work is certainly deemed routine.

The Applicants' duty under the US Patent Law is to teach how to **practice** the claimed invention. Applicants are unaware of any requirements that specify the duty to carry out specific experiments in order to obtain a US Patent. The Applicants believe that they have taught one of ordinary skill in the art how to practice the claimed invention. Through bacterial data they have demonstrated that the mutants produce a gene product that is glyphosate resistant and allows the host to grow in a normal fashion. To force the Applicants to produce plant experiments would mean that the Applicants would literally have to wait for years before filing a patent application in the plant arts because of the nature (time) of plant tissue culture and plant regeneration and resources available to the Applicant. This unreasonable burden would frustrate the basic underlying policy of the US Patent system to encourage early disclosure of technology to further science. As long as an Applicant teaches how to practice the invention she/he should be able to procure a patent. Applicants believe that they have taught one of ordinary skill in the art how to practice the claimed [illegible]

102 Rejection – Hawkes et al

Claims 1-23 have been rejected under 35 USC 102(a) as being anticipated by Hawkes et al WO 98/54330. The undersigned attorney just recently received the present case from the assignee Valigen (US) Inc. Prior to this the present application was being prosecuted by another law firm. The applicants hereby notify the Examiner that Valigen (US) Inc. is the common assignee of the present application and the Hawkes et al WO 98/54330 which includes a US counterpart SSN 09/424,344 filed 11/22/99.

102/103 Rejection – Lebrun et al WO 97/04103

Claims 1-13 and 20-23 have been rejected under 35 USC 102(b) as anticipated by Lebrun et al or in the alternative, under 35 USC 103(a) as obvious over Lebrun et al. This rejection is respectfully traversed.

The Lebrun et al reference does not anticipate any of the presently pending claims. The Lebrun et al reference involves the **transformation** of heterologous mutant EPSPS genes resulting in **TRANSFORMED** plants that contain an **INSERTED** gene. The inserted mutant gene must be highly expressed in order to render the transgenic plant herbicide resistant. The presently pending claims cover modified **NON-TRANSGENIC** plants. See the discussion in the Specification in Section 2.1 especially the passages on page 2 and 3 where it is acknowledged that **TRANSFORMED** plants containing mutant EPSPS genes are well known in the art.

The Lebrun et al reference cannot render the present claims obvious either. By transforming a plant with a mutant transgene the resultant transgenic plant expresses both the native EPSPS gene product and the mutant EPSPS gene product. A modified non-transgenic plant of the present invention contains only the native gene which has been mutated *in vivo*. Nothing in Lebrun et al would [illegible] Respectfully submitted

103 Rejection – Kmiec '325 in View of Lebrun et al

Claims 1-23 have been rejected under 35 USC 103(a) as being unpatentable over Kmiec US Patent 5,756,325 in view of Lebrun et al WO 97/04103. This rejection is respectfully traversed.

Kmiec '325 is acknowledged in the Specification as a prior art reference disclosing the use of gene repair technology to make mutations in genes *in vivo*. The Examiner is correct in stating that Kmiec '325 does not disclose the EPSPS gene. As described above in the preceding section of this response (which is incorporated herein by reference), Lebrun et al cannot support an obviousness rejection of the present claims either alone or in combination with Kmiec '325. There is no incentive for a skilled artisan to combine the **gene repair** technology of Kmiec '325 with the **transformation** technology of Lebrun et al. In fact these two technologies are in most respects considered opposites although the delivery of nucleotides into a cell would be similar. Gene repair would be used INSTEAD of transformation.

In view of the above it is respectfully requested that the present 103(a) rejection be withdrawn.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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Signed: Elaine E. Calimquim

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Please cancel Claim 24.

The claims are amended as follows:

WE CLAIM:

1. (As Amended) A modified non-transgenic herbicide resistant plant, which plant expresses a mutant EPSPS gene product and which plant has substantially normal growth as compared to a plant expressing the wild-type EPSPS gene product.

2. (As Amended) A modified non-transgenic herbicide resistant plant, which plant expresses a mutant EPSPS gene product, which gene product has substantially the same level of catalytic activity as compared to the wild-type gene product.

14. (As Amended) A method for producing a non-transgenic herbicide resistant or tolerant plant comprising

a. introducing into a plant cell a recombinacenic oligonucleobase to produce a mutant EPSPS gene; [and]

b. identifying a cell having a mutated EPSPS gene, which cell has substantially normal growth as compared to a corresponding wild-type plant cell; and

c. regenerating a non-transgenic herbicide resistant or tolerant plant from said plant cell.

15. (As Amended) A method for producing a non-transgenic herbicide resistant or

a. introducing into a plant cell a recombinagenic oligonucleobase to produce a mutant EPSPS gene; [and]

b. identifying a cell having a mutated EPSPS gene, which encoded mutant EPSPS protein has substantially the same catalytic activity as compared to a corresponding wild type EPSPS protein[.]; and

c. regenerating a non-transgenic herbicide resistant or tolerant plant from said plant cell.

19. (As Amended) The method according to claim 14 or 15 in which the mutant EPSPS gene is mutated at one or more amino acid positions, said positions selected from the group consisting of Leu_{173}, Gly_{177}, Thr_{178}, Ala_{179}, Met_{180}, Arg_{181}, Pro_{182}, Ser_{98}, Ser_{255}, and Leu_{198} in *Arabidopsis* or at an analogous amino acid residue in an EPSPS paralog.

20. (As Amended) The [plant] method according to claim 19 in which the positions in the *Zea mays* paralog are selected from the group consisting of Leu_{97}, Gly_{101}, Thr_{102}, Ala_{175}, Met_{104} Arg_{105} Pro_{106}, Ser_{23}, Ser_{179}, and Leu_{122}.

21. (As Amended) The [plant] method according to claim 19 in which the positions in the *Brassica napus* paralog are selected from the group consisting of Leu_{169}, Gly_{173}, Thr_{174}, Ala_{175}, Met_{176}, Arg_{177}, Pro_{178}, Ser_{94}, Ser_{251} and Leu_{194}

22. (As Amended) The [plant] method according to claim 19 in which the positions in the *Petunia hybrida* are selected from the group consisting of Leu_{169}, Gly_{173}, Thr_{174}, Ala_{175}, Met_{176}, Arg_{177}, Pro_{178}, Ser_{94}, Ser_{251} and Leu_{194}.

23. (As Amended) The [plant] method according to claim 14 or 15 in which the plant is selected from the group consisting of [illegible] grapefruit, tall grasses and *Brassica sp.*